REVIEW ARTICLE

Toxoplasma gondii infection in pregnant women in China

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SUMMARY

Toxoplasmosis, caused by the protozoan parasite *Toxoplasma gondii*, is one of the most common parasitic infections in humans. Primary infection in pregnant women can be transmitted to the fetus leading to miscarriage or congenital toxoplasmosis. Carefully designed nationwide seroprevalence surveys and case-control studies of risk factors conducted primarily in Europe and America, have shaped our view of the global status of maternal and congenital infection, directing approaches to disease prevention. However, despite encompassing 1 in 5 of the world's population, information is limited on the status of toxoplasmosis in China, partly due to the linguistic inaccessibility of the Chinese literature to the global scientific community. By selection and analysis of studies and data, reported within the last 2 decades in China, this review summarizes and renders accessible a large body of Chinese and other literature and aims to estimate the seroprevalence in Chinese pregnant women. It also reviews the prevalence trends, risk factors, and clinical manifestations. The key findings are (1) the majority of studies show that the overall seroprevalence in Chinese pregnant women is less than 10%, considerably lower than a recently published global analysis; and (2) the few available appropriate studies on maternal acute infection suggested an incidence of 0·3% which is broadly comparable to studies from other countries.

Key words: *Toxoplasma gondii*, Chinese pregnant women, seroprevalence, risk factors, China, pregnancy.

INTRODUCTION

China is home to 1 in 5 people on this planet and yet there are considerable gaps in the global scientific understanding of how infectious diseases in China are viewed in the global perspective. This review aims to focus specifically, on *Toxoplasma gondii* with respect to pregnant women in whom it has the potential to cause significant disease in the developing fetus and newborns. *T. gondii* is an obligate intracellular protozoan that belongs to the phylum Apicomplexa and probably infects all warm-blooded animals including humans (Tenter *et al.* 2000). Humans acquire *Toxoplasma* infection through consuming raw or undercooked meat, contact with cat feces, ingesting contaminated food or water, vertical transmission across placenta to fetus, or rarely through transplantation of a contaminated organ (Montoya and Liesenfeld, 2004). Infection in humans may cause various clinical manifestations. Adults with a normal immune system usually have few symptoms or mild and transient symptoms such as fever, malaise, and lymphadenopathy. Toxoplasmatic encephalitis and disseminated toxoplasmosis have been reported in AIDS, transplant recipients and people with immunodeficiencies due to immunosuppressive therapy or Hodgkin's disease (Luft and Remington, 1992; Weiss and Dubey, 2009). Immunocompetent women infected with *T. gondii* prior to conception

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have little or no risk of transmitting the infection to their fetus except those who become infected shortly before gestation (Vogel *et al*. 1996). Vertical transmission occurs in most cases when a mother has a primary infection during pregnancy and this can present itself as either subclinical infection or congenital toxoplasmosis with a wide spectrum of severe manifestation in newborns or relapse later in life (Weiss and Dubey, 2009; Hide *et al*. 2009).

The global status of *Toxoplasma* seroprevalence in pregnant women has recently been summarized and evaluated by Pappas *et al*. (2009). The incidence of congenital toxoplasmosis varies between 1 and 10 per 10000 live births in western countries: 0·8 /10000 births in the United States (Guerina *et al*. 1994), 3·4/ 10000 in the United Kingdom (Gilbert *et al*. 2006) and 4/10000 in Denmark (Lebech *et al*. 1999). Raw or undercooked meat was found to be the main risk factor in a European multicentre case-control study (Cook *et al*. 2000) as well as in another study from the United States (Jones *et al*. 2009).

With a population of 1·34 billion encapsulated within the world population of 6·8 billion, 1 in 5 people live in China. However, epidemiological knowledge regarding the prevalence and risk of associated maternal *Toxoplasma* infection is limited in China. The effect of this is to hamper efforts towards global estimation of disease burden, national evaluation of the current situation in China and the formulation of effective health policies nationally and globally. Although studies have been conducted in China, these are typically published in Chinese and consequently are largely inaccessible to the global scientific community whose international scientific language is English. To render this data more accessible, this review aims to gain a collective estimate of the nationwide seroprevalence of *T. gondii* infection in Chinese pregnant women, to review the prevalence trends, sources of risk and clinical manifestations in mothers and their fetuses/newborns. Thus providing an update on the current status of *Toxoplasma* prevalence in pregnant women in this major component of the global population.

SEARCH STRATEGY AND SELECTION CRITERIA

The primary search for literature was performed in PubMed and the ISI Web of Knowledge with keywords 'congenital toxoplasmosis' OR '*Toxoplasma* infection in pregnant women' AND 'China'. A search of JSTOR was conducted for outdated publications. Databases of Chinese publications, CNKI (China National Knowledge Infrastructure, http://www.cnki.net) and Wanfang (http://www.wanfangdata.com.cn), were subsequently searched for more articles with data on nationwide or provincial seroprevalence in China; the keywords for searching were 'Toxoplasma infection' AND (pregnant women' OR 'pregnancy'). The majority of these latter papers were published in Chinese and, therefore, probably not generally accessible to the English-speaking scientific community. A comprehensive search has been conducted up to December 2010 and relevant articles and book chapters, falling within our specified criteria (see below) both in English and Chinese are referenced.

For seroprevalence data in China, articles that were published in the last 2 decades, i.e. from January 1990 through December 2010, were retrieved. For a study to be included in the discussion, the minimum sample size was selected as 100. Studies that focused on pregnant subpopulations with potentially biased obstetric histories or that employed biased sampling were excluded from our seroprevalence estimations.

SEROPREVALENCE

Seroprevalence in China

The national survey of parasitic disease conducted by the Ministry of Health of China from 2001 to 2004 provides the latest prevalence data of general *Toxoplasma* infection in China. A seropositivity rate of 7·97% was measured for the general population from a sample of 47 444 people (Xu *et al*. 2005). This figure is lower than seen in many serological studies elsewhere (Jones *et al*. 2007). To our knowledge, however, there has been no nationwide epidemiological study or seroprevalence investigation of *Toxoplasma* infection in Chinese pregnant women. Nevertheless, serological testing for *Toxoplasma*-induced antibodies has been available to pregnant women for antenatal care or counselling in some hospitals and clinical laboratories in China. In reports of studies we retrieved which were conducted over the last 2 decades, a total of 56 have documented the seropositivity rate of women whose serum samples were collected during pregnancy. These were predominantly tested by ELISA to detect *Toxoplasma*-specific IgG (Table 1). The studies cover a wide range of districts including 20 of the total of 34 provinces (municipalities) in China.

The reported seroprevalence, ranging from 0·17% (Li *et al*. 2001) to 31·06% (Lin *et al*. 2008), displays considerable variance among districts, even among studies in the same region (Table 1). Therefore, no single provincial or district survey could reflect the nationwide seroprevalence in pregnant women. Although most of the studies included in this review (43 out of 56) reported seropositivity within the range of 0–10% and nearly half of them (20 of 43) reported rates of lower than 5%. It is notable that the 2 multi-year studies, both with largest sample sizes (1 of 18127 from Hubei and 1 of 10939 from Zhejiang), both reported seroprevalence rates around 10% in women during pregnancy (Liu and Yao, 2003; Suo and Yao, 2009). Though ranging widely between 0 and 10%, seroprevalence data from China show a

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Table 1. Seroprevalence of *Toxoplasma gondii* in Chinese pregnant women (data collected from publications from 1990 to 2010)

Period	Province	Sample size	Seroprevalence (%)	Age	Assay	TORCH	Reference
1992–1994	Anhui	1203	8·97	20–34	IHA	N	(Tang *et al*. 1994)
2004·5–2008·8	Beijing	4692	1·9	20–45	CLIA	Y	(Li *et al*. 2009)
2005·6–2005·11	Beijing	500	0·2	na	ELISA	Y	(Zhao *et al*. 2006)
1992–1994	Gansu	850	5·86	20–32	IHA	N	(Li P *et al*. 1994)
1993·4–1995·10	Gansu	1250	7·28	20–39	IHA	N	(Zhang *et al*. 1997)
1991·5–1991·8	Guangxi	786	8·14	16–36	IHA	N	(Lv *et al*. 1995)
1996·1–1997·10	Guangxi	810	5·93	na	IHA	N	(Guo *et al*. 1998)
1993·3–1995·6	Guizhou	607	5·77	16–47	ELISA	Y	(Guo *et al*. 1997)
1996·10–1998·6	Guizhou	1250	8·32	20–44	ELISA	N	(Zhang *et al*. 1999)
2000·3–2006·6	Guizhou	524	10·3	24–38	ELISA	N	(Zheng, 2007)
2005–2006	Guizhou	769	9·36	20–40	ELISA	N	(Tang *et al*. 2007)
2004–2005	Heilongjiang	1383	9·6	na	ELISA	N	(Zhang *et al*. 2006)
1993	Henan	449	2·89	na	IHA	N	(Li RP *et al*. 1994)
2004·10–2005·6	Henan	1400	7·5	20–44	ELISA	N	(Liu and Guo, 2009)
1998–2001	Hubei	2845	6·36	21–35	ELISA	N	(Chen *et al*. 2002)
2001·1–2007·12	Hubei	18127	11·78	na	ELISA	N	(Suo and Yao, 2009)
2002·1–2004·12	Hubei	4310	7·49	na	ELISA	N	(Chen *et al*. 2005)
2003	Hubei	530	10·9	na	ELISA	N	(Xu and Zhong, 2004)
2005·2–2005·3	Hubei	202	22·8	20–38	ELISA	Y	(Liu and Jun, 2009)
1991·9–1992·10	Hunan	1396	5·44	21–35	IHA	N	(Li LZ *et al*. 1994)
1997·6–1999·12	Hunan	2234	6·03	23–38	ELISA	N	(Lin *et al*. 2001)
1998*	Hunan	412	10·92	17–40	IHA	N	(Yang, 1998)
2001–2003	Hunan	124	6·45	na	ELISA	N	(Xiong *et al*. 2005)
2001·8–2004·4	Jiangsu	2503	0·84	21–39	ELISA	N	(Wu, 2004)
2003·6–2004·12	Jiangsu	2419	1·12	na	ELISA	N	(Luo *et al*. 2005)
2007·6–2008·5	Jiangsu	124	6·45	21–35	ELISA	Y	(Wang and Li, 2008)
1992·3–1995·12	Jiangxi	2076	7·8	20–38	IHA	N	(Huang, 1996)
2006	Jilin	235	10·6	21–38	ELISA	N	(Liu *et al*. 2009)
2000·11–2001·5	Liaoning	405	21·5	20–47	ELISA	N	(Liang *et al*. 2004)
2008·9–2009·12	Liaoning	359	0·5	24–37	ELISA	Y	(Liu and Wei, 2010)
1999*	Ningxia	303	6·9	na	IHA	N	(Zhao *et al*. 1999)
1997·2–1998·12	Shandong	800	2·25	22–31	ELISA	N	(He *et al*. 1999)
1998·6–1999·8	Shandong	2000	2·8	22–32	ELISA	N	(Liu and Li, 2001)
1992·2–1992·5	Shanghai	222	14·4	20–39	ELISA	N	(Liu *et al*. 1995)
1992·6–1994·12	Shanghai	1818	3·25	na	ELISA	N	(Ao *et al*. 1996)
1998	Shanghai	356	9·27	na	ELISA	N	(Gu and Yu, 1998)
2002·4–2003·10	Shanghai	1075	3·26	21–44	ELISA	N	(Jiang *et al*. 2005)
2009·1–2009·10	Sichuan	720	11·94	na	ELISA	N	(Huang *et al*. 2010)
2004·4–2005·1	Taiwan	483	9·11	na	ELISA	N	(Hu *et al*. 2006)
2007*	Taiwan	426	31·06	15–49	ELISA†	N	(Lin *et al*. 2008)
1989–1990	Tianjin	8953	3·4	na	IHA	N	(Lu, 1992)
1990–1991	Zhejiang	519	4·8	20–35	ELISA	N	(Yu *et al*. 1994)
1991·4–1991·10	Zhejiang	709	10·72	na	ELISA	N	(Pan *et al*. 1992)
1994·1–1994·12	Zhejiang	3717	8·74	na	ELISA	N	(Chen and Zhang, 2000)
1996	Zhejiang	3918	10·82	na	ELISA	N	(Zhang, 1996)
1996–1997	Zhejiang	284	4·58	21–36	ELISA	N	(Xu *et al*. 2001)
1996–2000	Zhejiang	8321	0·32	20–45	ELISA	N	(Lin, 2001)
1998–2002	Zhejiang	10939	9·23	19–45	ELISA	N	(Liu and Yao, 2003)
1999·1–2002·12	Zhejiang	1368	0·95	21–39	ELISA	N	(Pan, 2005)
2002·3–2005·9	Zhejiang	5686	2·13	na	ELISA	N	(Zhou and Wu, 2007)
2004–2007	Zhejiang	2772	1·66	na	ELISA	N	(Qiu *et al*. 1997)
2006·1–2007·5	Zhejiang	5103	1·3	na	ELISA	Y	(Qian *et al*. 2008)
2006·1–2008·12	Zhejiang	9837	3·71	18–41	ELISA	Y	(Chen and Lu, 2010)
2007·1–2010·8	Zhejiang	1751	0·17	18–40	ELISA	Y	(Li *et al*. 2001)
2007·12–2008·10	Zhejiang	1491	6·51	na	ELISA	N	(Ji *et al*. 2009)
2008·1–2008·12	Zhejiang	1220	3·01	20–46	ELISA	Y	(Liu and Lu, 2010)

Note:
Period: during which sera samples were collected from pregnant women, documented in the referred study. *: the publication year of the study when no specific period is documented in it.
Age: na, the age range of women that attended in the study is not mentioned.
Assay: applied in the study for determination of past infection. IHA: indirect hemaglutination; ELISA: enzyme-linked immunosorbent assay; CLIA: chemiluminescent immunoassay. For the studies applying IHA, a titre of greater than 1:64 is generally considered as positive; for the rest, only one of the 44 studies using ELISA reported a concrete cut-off value of >35I U/ml, highlighted with † and the only CLIA study reported a cut-off value of >6I U/ml.
TORCH: prenatal testing for infection of *Toxoplasma*, Rubella, Cytomegalovirus, Herpes simplex; Y = data from TORCH test; N = data from test specifically for *Toxoplasma* infection.

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relatively low level compared with seroprevalence reported from other countries (both neighbouring and cross-continental) most of which had prevalences above 10% with some up to 60% and beyond (Pappas *et al*. 2009). This low seroprevalence in Chinese pregnant women suggests that there might be only a small proportion of women who are immune to *Toxoplasma* infection prior to gestation leaving the majority to be susceptible to infection during pregnancy.

Infection has been thought to be more common in warmer and humid areas or at lower altitudes (Elsheikha, 2008). So far, however, we found no studies or data that investigate this potential influence on *T. gondii* seroprevalence in China. It could be a very important project to be carried out as conditions can vary very widely across the large expanse occupied by China. Such results will also be very useful for understanding the true *T. gondii* infection status of pregnant women and may influence regional healthcare policy.

Seroprevalence trends

Among the studies that had collected samples for more than 5 years, only 1 provided annual data on cases and seroprevalence (Suo and Yao, 2009). Each year from 2001 to 2007, pregnant women in Wuhan were tested for *Toxoplasma*-specific antibodies in serum by ELISA (IgM and IgG) at the time of their prenatal examination (Table 2) (Suo and Yao, 2009). Overall, the proportions of seropositive mothers (either IgM and IgG positives or IgG only) showed a slightly increasing trend. No significant difference was observed between any individual years except that the prevalence of the IgG-only positives in 2007 were significantly increased when compared with the figures for 2001.

For the general population in China, *T. gondii* seropositivity was reported to be 4·86% ($n=61\,494$) from the 1983 ~ 1986 nationwide survey (Cui, 1991) and a higher rate of 7·97% (n = 47 444) was found in the 2001 ~ 2004 nationwide survey (Xu *et al*. 2005) showing an upward trend. By comparison, seroprevalence of *T. gondii* infection in China, either for the general population or for the subgroup of pregnant women, in these Chinese studies has not shown the decreasing trend that has been reported in the USA (Jones *et al*. 2007) or some other western countries during recent years (Pappas *et al*. 2009). The reasons for this will be discussed in a later section of this paper.

SEROLOGICAL DIAGNOSIS OF ACUTE INFECTION DURING PREGNANCY

Women that show seronegativity for *Toxoplasma*-induced antibodies before or early in pregnancy are at risk of acquiring acute infection and passing it to their fetuses transplacentally. Rarely, transplacental transmission can also occur in chronically infected women who are immunocompromised due to HIV/AIDS or immunosuppressive treatment and experience re-activated infection (Montoya and Remington, 2008). Most pregnant women do not show obvious symptoms when infected acutely (Boyer *et al*. 2005) and, therefore, serological testing is crucial to the diagnosis of acute infection during pregnancy (Montoya and Remington, 2008).

Table 2. The yearly *Toxoplasma*-specific seropositivity in pregnant women reported from Wuhan during 2001 ~ 2007 by Suo and Yao (2009)

		Seropositivity	
Year	*N*	IgG +, IgM + (%)	IgG +, IgM − (%)
2001	2181	1·05	6·92
2002	2198	1·23*	7·01*
2003	2151	1·16*	7·53*
2004	1917	1·36*	7·46*
2005	2154	1·53*	7·89*
2006	3260	1·63*	8·04*
2007	4266	1·69*	8·35†

* The rate showed no significant difference compared with that of any previous studied year.
† The seropositive rate is significantly higher compared with that of 2001, $P<0·05$.

Immunological testing for IgM seropositivity

For clinical diagnosis, as practiced by most of the Chinese studies included here, seropositivity of IgM is interpreted as a recent or acute infection. This is because *Toxoplasma*-specific IgM usually develops early during primary infection and generally decreases to below the detection cutoff within months after infection (Jenum and Stray-Pedersen, 1998). However, *T. gondii*-specific IgM can sometimes persist for years, giving rise to false-positive diagnoses of acute infection when no additional tests for *T. gondii*-specific IgG were conducted, prior to conception or in the first trimester, to exclude women already infected before pregnancy (Jenum *et al*. 1998; Montoya, 2002). Essentially, a positive specific-IgM in a single serum sample can be interpreted as a true-positive result of recent or acute infection, a true-positive result after an infection acquired in the distant past or a false-positive result (Montoya, 2002). The data from studies that only report IgM seropositivity are not valid and, hence, excluded from this discussion of the primary *Toxoplasma* infection during pregnancy in Chinese women.

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Table 3. Seropositivity based on a combination of tests for *Toxoplasma*-specific IgG, IgM and CAg in pregnant women

Period	District	*N*	IgG+, IgM+, CAg− (%)	IgG+, CAg+, IgM− (%)	IgM+, CAg+, IgG− (%)	IgM+, CAg+, IgG+ (%)	IgM+, CAg+ (%)	Ref
1994·1–1994·12	Zhejiang	3717	0·24	0·11	0·13	0·08	0·21	(Chen and Zhang, 2000)
1996–2000	Zhejiang	8321	0	0	0·19	0	0·19	(Lin, 2001)
1997·2–1998·12	Shandong	800	0·25	0	0·5	0	0·5	(He *et al*. 1999)
1998·6–1999·8	Shandong	2000	0·75	0	1·2	0	1·2	(Liu and Li, 2001)
1998–2001	Hubei	2845	0·28	0·35	0·25	0·04	0·29	(Chen *et al*. 2002)
1998–2002	Zhejiang	10 939	0	0·04	0·19	0	0·19	(Liu and Yao, 2003)
2001·8–2004·4	Jiangsu	2503	0	0·04	0·84	0	0·84	(Wu, 2004)
2005–2006	Guizhou	769	0·13	0·91	0·13	0	0·13	(Tang *et al*. 2007)
2009·1–2009·10	Sichuan	720	0	0	0·14	0	0·14	(Huang *et al*. 2010)
Total		32 614					0·32	

Note: IgM+, IgG+, CAg+, refer to the seropositivity in the detection of *Toxoplasma*-specific IgM, IgG and circulating antigen, respectively; for each row, the seropositivity rate shown in the column 'IgM+ CAg+' is derived from the addition of the rate in the column of 'IgM+, CAg+, IgG−' and the rate in the column of 'IgM+, CAg+, IgG+'.

Combining immunological testing for IgM, IgG and CAg

Serological evidence of acute infection by *Toxoplasma*, as described by Lebech *et al*. (1996), requires (i) seroconversion, (ii) a significant increase of both specific-IgG titre (>3-fold) and dye test titre (⩾4-fold) and (iii) the presence of specific-IgM and a high IgG titre (dye test result, ⩾300 IU/ml). However, this standard is hardly ever adopted outside of reference laboratories. No one study in our survey has consistently applied this standard to the diagnosis of primary pregnant infection. Studies that combined tests of IgM, IgG and CAg in diagnosis, though limited, are the most informative since they provided data that could be measured against the current Chinese serological standard for diagnosis of acute *Toxoplasma* infection (established by the Forth National Toxoplasmosis Symposium) (Gan, 2001): (i) specific-IgG positivity and a significant increase of specific-IgG titre (⩾4-fold) in 2 weeks, (ii) specific-IgM (IgA) positivity and (iii) detection of CAg. Acute infection can be determined when 2 of the former conditions are met.

We retrieved 9 studies that used these combined seropositivity data (Table 3). As none of these studies have collected follow-up samples to detect the change in specific IgG titre, a serum sample can be assumed to be acutely infected only when both specific IgM and CAg show positivity. The rates of both IgM and CAg positivity (shown in the column of 'IgM+, CAg +' in Table 3) are within 0·3% in most studies (6 of 9). The 3 higher outliers (0·5%, 0·84% and 1·2%) demonstrate that there may be some local variation in prevalence. The average seropositivity of IgM combined with CAg is 0·33% throughout the 9 studies. Therefore, around 0·3% of the studied women can be considered to be diagnosed with acute infection during pregnancy according to the national standards currently used in China. This is an estimate of the level of incidence of infection in pregnant women. A comparable incidence (0·19%) was reported from a nationwide prospective study of 35 940 pregnant women in Norway (Jenum *et al*. 1998) where the seroprevalence of *Toxoplasma* infection is 10·9% among pregnant women and is approximately comparable to the seroprevalence in Chinese pregnant women estimated from our studies.

RISK FACTORS

Several potential risk factors associated with *Toxoplasma* infection have been investigated in Chinese pregnant women. According to a study, from Changchun (in the north of China) in 2008, major risk factors identified by multivariate analysis include eating raw or undercooked meat, unwashed raw vegetables or fruit, contact with cats, living in rural areas and low educational level (Liu *et al*. 2009) (Table 4).

Consumption of raw or undercooked meat

Consumption of raw or undercooked meat was found to be a strong risk factor with an odds ratio (OR) of

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Table 4. Risk factors associated with *Toxoplasma* infection in Chinese pregnant women as reported by Liu *et al*. (2009)

Risk factor	Odds ratio	95% CI	*P*-value
Consuming raw or undercooked meat	5·69	1·14–16·23	0·008
Unwashed raw vegetable or fruit consumption	3·85	1·06–9·63	0·015
Contact with cats	8·23	0·85–57·63	0·001
Residence of rural area	4·81	0·54–4·64	0·006
With no education	4·93	1·02–12·65	0·044

5·69 (95% CI: 1·14–16·23) as mentioned in the study by Liu *et al*. (2009) and consistent with the findings from other countries (Kapperud *et al*. 1996; Cook *et al*. 2000; Jones *et al*. 2009). This food-borne feature of *T. gondii* infection may partially explain the relatively low seroprevalence reported in China as consumption of raw or undercooked meat is not as common in the Chinese daily diet as in some Western diets. With regard to the kinds of meat consumed, Li and Wu (2002) reported that subjects favouring duck and beef were associated with higher seropositivity than those with a preference for other kinds of meat including pork, lamb and chicken. However, such details may vary by region, dependent on local dietary customs. As reported in western countries, undercooked lamb and pork are major dietary risk factors in Norway, with beef and lamb being major factors in France and the United States (Kapperud *et al*. 1996; Cook *et al*. 2000; Jones *et al*. 2009). Poor kitchen hygiene and improper handling of raw meat may also lead to cross-contamination of foods resulting in additional risk beyond meat consumption (Kapperud *et al*. 1996; Cook *et al*. 2000).

Contact with or ownership of cats or dogs

Contact with cats was found with the highest odds ratio, 8·23 (95% CI 0·85–57·63) in Liu's study (Liu *et al*. 2009) (Table 4) although there are discrepancies between this study and the conclusions of some studies from different countries (Kapperud *et al*. 1996; Cook *et al*. 2000). Occasional contact with or ownership of cats may not necessarily be a risk factor, whereas frequent exposure to feline feces or neglect of preventive measures (i.e. not washing hands or wearing gloves) may increase the risk of infection to an appreciable level. In the latest study from the United States, Jones *et al*. (2009) indentified that having 3 or more kittens increased the risk while having 1 or 2 did not. Pets and livestock kept together with cats are highly exposed to oocysts in the feces of infected cats, thus becoming another potential source of infection by transportation of oocysts into households. Evidence for this is presented by Huang who studied a sample of 2076 pregnant women in Guangxi (Southwest of China) and found a significantly higher seropositivity rate in pregnant women owning dogs compared with those with no dogs in houses (Huang, 1996). In a study from Panama, dog contact was observed with a risk ratio even higher than that of the above study. Contact with cat and dog fur contaminated with cat feces was suggested as a vector for transmission to people without careful preventive measures (Frenkel *et al*. 1995). A recent study in Lanzhou (Northwest China) reinforces this view by demonstration of a high prevalence of *Toxoplasma* infection in dogs (Wu *et al*. 2011).

Consumption of unwashed raw vegetables or fruits and farming as an occupation

Widespread infectious oocysts also contribute to a range of potential risk factors for *T. gondii* infection, including contact with soil, eating unwashed contaminated vegetables and fruits, and drinking unpasteurized milk or untreated surface water. Consumption of unwashed raw vegetables and fruits was found to be associated with *Toxoplasma* infection during pregnancy (ORs: 3·85; 95% CI: 1·06–9·63) by Liu *et al*. (2009). Gardening or contact with soil has been identified as a risk factor in several case-control studies (Kapperud *et al*. 1996; Cook *et al*. 2000). In China, farmers are the population with the most frequent contact with soil and also may have significant contact with unpasteurized milk. A recent study, showing high prevalences of infection in dairy goats, suggests a potential risk of a transmission route of *Toxoplasma* via unpasteurized milk (Zhao *et al*. 2011). Significantly higher seropositivity has been reported in pregnant women working on farms than with other occupations (Yu *et al*. 1994; Sun *et al*. 2006) and being an agricultural worker has been identified as promoting a higher risk of maternal infection in Taiwan (Hu *et al*. 2006). Therefore, women on farms are suggested to be at an increased risk of *Toxoplasma* infection during pregnancy.

Living in rural regions

Living in rural or suburban regions is another risk factor for Chinese pregnant women and is supported by most studies that have available residence information of the women (Yu *et al*. 1994; He *et al*. 1999; Liu and Li, 2001; Wu, 2004; Li, 2007; Xu, 2007; Liu *et al*. 2009). This is consistent with the higher seroprevalence of *Toxoplasma* infection recorded in rural areas based on a global perspective (Pappas *et al*. 2009). Residence is not a univariate factor; in China rural or suburban residence is generally associated with poorer sanitary facilities, more frequent contact with soil or animals and drinking unpasteurized or unboiled water.

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Age and educational level

Two studies also suggest that women in China of lower educational level are more likely to acquire infection during their pregnancy (Sun *et al*. 2006; Liu *et al*. 2009). Liu and coworkers found that pregnant women who had not attended school were at higher risk of infection than women with schooling (Liu *et al*. 2009). Even the pregnant women who obtained middle school education showed a significantly higher seroprevalence of *Toxoplasma* compared to those with higher education (Sun *et al*. 2006). Both studies suggest health education as an effective intervention of *Toxoplasma* infection in pregnant women.

Age, on the other hand, is not found to be associated with *Toxoplasma* infection in Chinese pregnant women (Wu, 2004; Sun *et al*. 2006; Ji *et al*. 2007) although the general view is that the prevalence of *Toxoplasma* infection increases with age (Elsheikha, 2008).

MANIFESTATION IN MOTHERS AND FETUS/NEWBORNS

Transplacental transmission can cause miscarriage, stillborn fetuses, neonatal death, or fetal/newborn abnormalities. Pregnant women who are infected with *T. gondii* usually have absent or only mild symptoms; fever, malaise, extreme fatigue, myalgia, headache and lymphadenopathy were recorded as symptoms in maternal infection (Zhang *et al*. 1996; Jenum *et al*. 1998; Boyer *et al*. 2005). However, clinical manifestations in infected newborns can be severe, including chorioretinitis, strabismus, blindness, epilepsy, psychomotor or mental retardation, anaemia, jaundice, rash, petechiae of thrombocytopenia, encephalitis, pneumonitis, microcephaly, intracranial calcification, hydrocephalus, diarrhoea, and hypothermia (Remington *et al*. 2010). The incidence and severity of congenital infection mainly depend on the onset of maternal infection during pregnancy. Infection acquired in later gestation is more likely to result in vertical transmission; however, severe manifestation is more related to the infection in an early stage of pregnancy (Dunn *et al*. 1999; Montoya and Remington, 2008).

CONCLUSIONS

Serological data, collectively assembled in our study, show a relatively low prevalence of *Toxoplasma* infection among pregnant women in most areas of China compared to the global level. Despite the tendency towards lower seroprevalence in many western countries, no such decrease has been observed in the last 20 years in China. A nationwide survey or sophisticated study with large and representative sampling is therefore required imminently to establish an authentic prevalence and incidence of maternal *Toxoplasma* infection in China on which an efficient health promotion policy can be defined. For individual pregnant women at risk, adequate serum samples and clinical information for confirmation of seroconversion are essential to improve the diagnostic accuracy of primary infection and to facilitate follow-up for cases of maternal infection as well as congenital toxoplasmosis.

Maternal infection and congenital toxoplasmosis can be largely prevented if women and their health-care providers are better educated about *Toxoplasma* infection and the avoidance of risk. Pregnant women should avoid eating or tasting raw or undercooked meat. Preventive measures are suggested for pet owning, gardening and farming (i.e. wearing gloves and washing hands frequently). Kitchen hygiene should be improved, including avoiding drinking contaminated liquids or consuming inadequately washed vegetables and fruits. Education aimed at prevention is the most accessible and cost-effective method (Elsheikha, 2008) especially in China where seroprevalence is low and any screening programmes would be considerably expensive if adopted for large populations of non-immune pregnant women. Once prevention fails and acute infection occurs during pregnancy, treatment should be encouraged to reduce the transmission or the clinical severity of fetal infection. Effective prevention and treatment require the physician to have knowledge about the manifestations and treatment of toxoplasmosis as well as a general public awareness of the risks and consequences of maternal and congenital *Toxoplasma* infection.

Conflicts of interest

We declare that we have no conflicts of interest.

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